

M E M O R A N D U M

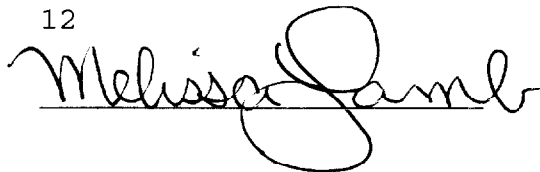
DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

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Date: October 12, 2000  
To: Dockets Management Branch (HFA-305)  
From: Melissa Lamb  
Office of Generic Drugs  
Subject: ANDAs

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: Blend Uniformity Analysis Draft Guidance  
Presented for: PQRI Workshop on Blend Uniformity  
Date Presented: September 7, 2000  
Presented by: Frank Holcombe, Jr., Ph.D.  
Number of Pages: 12

  
Melissa Lamb

Attachment

90S-0308

M691

# **PQRI Workshop on Blend Uniformity**

## **ANDAs: Blend Uniformity Analysis Draft Guidance**

**Frank O. Holcombe, Jr., Ph.D.  
Associate Director for Chemistry  
Office of Generic Drugs, CDER**

**September 7, 2000**

## **Background:**

- **In-Process Controls for ANDAs**
- **Applicant Questions/Complaints to  
OGD Management**
- **Internal Discussion/External Evaluation**
- **Consistent Review Practice Defined**
- **Guidance (for Industry) Developed**
- **Draft Guidance for Industry Published  
(8/99)**

## **Guidance Contents:**

- **Intended for ANDAs (Original and Certain Supplements)**
- **Used 21 CFR 211 and 21 CFR 314 (Relating to In-Process Controls)**
- **Described Extent of Coverage for Dosage Forms, Composition**
- **Described Sampling and Test Acceptance Criteria**

## **Guidance Contents:**

- **Coverage Included Application and Production Batches**
- **Based in Part on USP Content Uniformity Chapter**
- **Complex Products Addressed on Case by Case Basis**
- **Was an Application, Not a GMP Requirement**

## **Guidance Contents - Sampling:**

- **NMT 3X Dosage Unit Weight**
- **Increase to NMT 10X**  
**(if Sampling Bias Demonstrated)**
- **Sampling Locations not Restricted (Blender or Containers)**
- **Six to Ten Samples, No Composites**
- **Analysis Sample Equivalent to One Dosage Unit Weight**

## **Guidance Contents - Analysis:**

- **Individual, Mean, RSD**
- **Range of Mean - 90% - 100%**
- **RSD NMT 5.0%**
- **Multi-Tier Testing Not Recommended**

## **Background:**

- **Comments Received**
- **Internal Evaluation/Discussions**
- **Unexpected Level of Reaction to Guidance**
- **Ongoing Revision**
- **Involvement with PQRI**
- **PQRI Drug Product Technical Committee  
Priority**
- **PQRI Workshop**



## **Issues/Concerns:**

- **Concepts**
  - **Use Beyond ANDAs**
  - **Differences Between NDA and ANDA**
  - **Deletion of Testing Requirement**
  - **Inappropriate Test for Validated Process**
  - **Center Review or Field GMP Issue**

## **Issues/Concerns:**

- **Technical Areas**
  - **Problems Inherent in Sampling of Solid Heterogeneous Systems**
  - **Sample Sizes**
  - **Analytical Sample Preparation**
  - **Treatment of OOS Results / Multi-Tier Testing Procedures**
  - **Basis for Acceptance Criteria**

## **Revision:**

- **Concepts**
  - **Use Beyond ANDAs - NO**
  - **Differences Between NDA and ANDA - Explanation**
  - **Deletion of Testing Requirement - Provision for Deletion**

## **Revision:**

- **Technical Areas**
  - **Sample Sizes - Relaxation of Recommendation**
  - **Analytical Sample Preparation - Relaxation of Recommended Sample Size**
  - **OOS Results - Potential Basis for Alternate Methods/Criteria for Homogeneity Demonstration**

## **Remaining Issues/Concerns:**

- **Problems Inherent in Sampling of Solid Heterogeneous Systems**
- **Inappropriate Test for Validated Process**
- **Multi-Tier Testing Procedures**
- **Basis for Acceptance Criteria**